12 11
~~30.~~ (new) The method of claim ~~29~~ wherein said thrombotic disease is selected from the group consisting of deep leg vein thrombosis, reocclusion after a bypass operation or angioplasty (PT(C)A), occlusion in peripheral arterial disease, pulmonary embolism, disseminated intravascular coagulation, coronary thrombosis, stroke, and the occlusion of a shunt or stent.

31. (new) A method for providing antithrombotic support in thrombolytic treatment utilizing rt-PA or streptokinase, which comprises administering a therapeutically effective amount of a compound according claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein E denotes an R_bNH-C(=NH)- group, or a physiologically acceptable salt thereof.

32. (new) A method for preventing metastasis or the growth of clot-dependent tumours, which comprises administering a therapeutically effective amount of a compound according claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein E denotes an R_bNH-C(=NH)- group, or a physiologically acceptable salt thereof.

33. (new) A method for treating or preventing fibrin-dependent inflammatory processes, which comprises administering a therapeutically effective amount of a compound according claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein E denotes an R_bNH-C(=NH)- group, or a physiologically acceptable salt thereof.

REMARKS

Claims 1-17 were pending but have been cancelled by amendment herein. New claims 18-33 have been added by amendment herein. Thus, claims 18-33 are now pending.

The previous Office action (mailed October 27, 1998) stated a restriction requirement. In response to this requirement, the applicants, in their previous communication (filed January 4, 1999) elected, without traverse, to prosecute claims directed to the invention of Group II. As discussed in that previous communication, Group II is understood by the applicants to encompass the compounds and compositions of claims 1-12, to the extent that Het is limited to benzimidazolyl and Ar is limited to phenyl, naphthyl or thienyl.

The previous action also required the election of a single disclosed species falling within the scope of the elected invention. The following species was elected:

1-Methyl-2-[N-[4-(N-n-hexyloxycarbonylamidino)phenyl]-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-ethoxycarbonylethyl)-amide.

In view of the species elected, it is the understanding of the applicants that they have, in effect, elected to prosecute claims directed to the invention of Group II, as defined above, wherein the definition of such group is further limited to compounds wherein R_3 is pyridyl, as in the elected species, and wherein R_2 does not include piperidinyl, as this is classified above the other ring systems present in the elected species and as a search for prior art compounds

containing piperidinly would thus impose undue burden. The Examiner is requested to confirm that this is also his understanding of the election made.

Finally, the previous action required that if Group II were elected that the method of use claims be limited to the antithrombotic use of claims 13 and 14, the tumor inhibitory use of claim 16 or the anti-inflammatory use of claim 17. The antithrombotic use of claims 13 and 14 was elected.

The current action states a modified restriction requirement, wherein a new invention, designated Group V1, is defined. Group V1 is understood to include compounds (e), (f), (g), (h), (l), and (m) of claim 6, as well as the single compounds identified in claims 8, 9 and 10. It is also understood that Group V1 includes the physiologically acceptable salts of claim 11, the pharmaceutical composition of claim 12 and the method of use of claims 13 and 14, to the extent that claims 11-14 are limited to compounds (e), (f), (g), (h), (l), and (m) of claim 6, as well as the single compounds identified in claims 8, 9 and 10. As compound (s) of claim 6 is the same as the compound identified in claim 9, compound (s) of claim 6 is understood to be included in Group V1, by implication.

It is noted that the nine compounds compounds specifically included in Group V1 fall within Group II. Consequently, it is applicants' understanding that Groups II and Group V1 are both within the permissible scope of election, that the Examiner has performed a search that is co-extensive not only with the nine compounds of Group V1 but also with Group II, and that claims directed to Group II, and not merely Group V1, are now under consideration. The Examiner is requested to confirm that this is also his understanding of the matter.

It is noted, with satisfaction, that the Examiner has stated that he has examined compounds (e), (f), (g), (h), (l), and (m) of claim 6, as well as the single compounds identified in claims 8, 9 and 10, and found them to be allowable.

To facilitate further prosecution claims 1-16 have been cancelled and replaced with new claims, 18-33, which are limited to the scope of Group II, as that group is defined above.

Except as noted below, new claims 18-22 are the same as cancelled claims 1-5, respectively, but Ar is limited to phenylene, naphthylene or thienylene; Het is limited to benzimidazolyl; R_3 is limited to pyridyl; and R_2 does not include piperidinyl. New claim 23 corresponds to cancelled claim 6 but includes only compounds (e), (f), (g), (h), (l), (m) and (s) thereof. There is presently no claim which corresponds to cancelled claim 7, as the compound identified by that claim does not fall within the scope of the election. Except as noted below, new claims 24, 25 and 26 are the same as claims 8, 9 and 10, which have been cancelled only to simplify the numerical ordering of the claims. Except as noted below, new claims 27-33 are the same as cancelled claims 11-17, but depend from new claims 18, 19, 20, 21, 22, 23, 24, 25 or 26, and are thus limited to elected subject matter. It is earnestly believed that the new claims are directed to a proper Markush group in that they are directed to the common nucleus of Group II.

It is believed that no change in inventorship is required by the amendment of the claims made herein.

The rejection of cancelled claims 6, 8-10, 13 and 14 under 35 USC 112, second paragraph, is noted. The use of the terms "double prodrug" and "salt" are two of the stated bases for rejection. These bases for rejection are dealt with by the new claims as follows:

(a) The new claims still employ the term "double prodrug", as it is urged that the meaning of this term is apparent. It is possible that the Examiner may not have noticed that this term is defined in the descriptive portion of the specification at page 5, lines 26-30. Should the Examiner continue to assert that use of the term "double prodrug" renders the claims improper under the second paragraph of Section 112, even though the term is defined in the application, it is requested that he provide reasons for such legal conclusion.

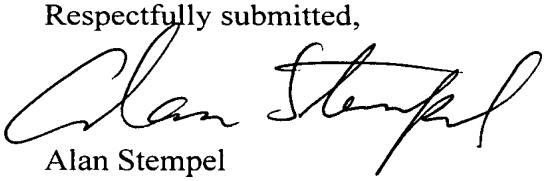
(b) To avoid rejection under Section 112, new claims 23, 24, 25 and 26 (and the claims which depend therefrom) are limited to *physiologically acceptable* salts.

Cancelled claim 13 stands rejected under 35 USC 112, second paragraph, because the term "preventing" is deemed to lack "propriety". It is noted that the term "preventing" is also employed in cancelled claims 16 and 17, although these claims were not rejected on this basis. New claims 29, 32 and 33 still employ the term because the Examiner has not put forth any specific reason why the term lacks propriety. It is pointed out that the term prevention is not understood by the medical community to connote the absolute and complete avoidance of a condition, something which might well be viewed as unattainable and impossible. Rather the term is understood to mean the significant reduction in the occurrence of a condition, something which is often quite attainable and possible. The United Stated Food and Drug Administration frequently approves labeling indicating that a given drug is to used for the "prevention" of a given condition. For example, the approved labeling for Persantine® (dipyridamole USP) indicates that this drug "is indicated as an adjunct to coumarin anticoagulants in the **prevention** of postoperative thromboembolic complications of cardiac valve replacement."

Some of the cancelled claims employed the phrases "may be", "may additionally be" and "may be cleaved". Although these phrases did not constitute bases for rejection, it is known that they are not viewed with favor by the Office. To avoid possible rejection under Section 112 on the basis of these phrases, the new claims instead employ the corresponding but more definite phrases "is optionally", "is optionally, additionally," and "is cleaved".

It is earnestly asserted that the claims now pending comply with the restriction requirement and elections made and avoid the stated grounds for rejection. It is thus urged that these claims are allowable and that the application as a whole is now in condition for allowance.

Respectfully submitted,



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Enclosures:
(1) Form PTO/SB/17
(2) Return post card